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## Surveillance of Patients with Metal-on-Metal Hip Resurfacing and Total Hip Prostheses

A Prospective Cohort Study to Investigate the Relationship Between Blood Metal Ion Levels and Implant Failure

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### LL ABSTRACT

**Background:** We designed a prospective, single-center study to assess whether blood metal ion levels could predict implant failure in patients managed with unilateral metal-on-metal hip resurfacing or total hip arthroplasty.

**Methods:** Five hundred and ninety-seven patients who had received unilateral Articular Surface Replacement prostheses at least twelve months earlier were recruited. Blood metal ion levels were compared between the group of patients with failed implants and the group with non-failed implants. Implant failure was defined as prostheses associated with revision, an intention to revise, or poor patient-reported hip function (Oxford Hip Score, <31 of 48). Specificity, sensitivity, area under the curve, positive and negative predictive values, and odds ratios were calculated. Logistic

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regression analysis was used to identify other risk factors for implant failure.

**Results:** Patients with failed arthroplasty had significantly higher blood cobalt and chromium ion levels than did patients with non-failed arthroplasty ( $p < 0.01$ ). Blood cobalt ion levels were disproportionately raised in patients with failed total hip arthroplasty (8.2  $\mu\text{g/L}$ ) compared with patients with failed hip resurfacing (2.5  $\mu\text{g/L}$ ) ( $p = 0.018$ ). Blood chromium ion levels were not significantly different in patients with failed total hip arthroplasty and failed hip resurfacing ( $p = 0.058$ ). The maximum value of either metal ion had good discriminant ability to predict implant failure (area under the curve, 0.76). A 7- $\mu\text{g/L}$  cutoff had a positive predictive value of 0.75 (95% confidence interval, 0.66 to 0.82) and a negative predictive value of 0.82 (95% confidence interval, 0.78 to 0.86). In patients managed with total hip arthroplasty, for each increase of 1  $\mu\text{g/L}$  there was a 23% ( $p < 0.001$ ) increase in the odds of them being in the failed group. For patients managed with hip resurfacing, the increase in odds was 5% ( $p < 0.001$ ).

**Conclusions:** Raised levels of blood metal ions were associated with failed metal-on-metal hip resurfacings and total hip arthroplasties. A threshold level of 7  $\mu\text{g/L}$  had inadequate sensitivity to be used in isolation as a screening test for implant failure, but it provided nearly optimal misclassification rates. No level had a perfect positive predictive value, and so we discourage surgeons from performing revision surgery based on blood metal ion levels alone. Levels of cobalt ions were raised out of proportion to levels of chromium ions in failed total hip arthroplasty and may reflect a different mechanism for metal ion generation.

**Level of Evidence:** Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

There have been recent high-profile recalls of breast<sup>1</sup> and orthopaedic<sup>2</sup> prostheses, prompting interest in post-market surveillance. The past decade has seen a surge in the use of metal-on-metal hip implants, as they appeared to be the optimal low-wearing and high-performance devices for younger, more active patients<sup>3</sup>. In 2008, approximately 35% of all hip replacements in

● A Prospective Cohort Study to Investigate the Relationship Between Blood Metal Ion Levels and Implant Failure

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the United States involved metal-on-metal implants<sup>3</sup>. However, in subsequent years there has been a decline in their use<sup>4</sup> amid concerns of unacceptable early failure rates and adverse responses to metal debris<sup>5</sup>.

In April 2010, the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) published a medical device alert to guide the surveillance of all types of metal-on-metal hip arthroplasty<sup>6</sup>. An “action level” of seven parts per billion ( $\mu\text{g/L}$ ) for cobalt or chromium was suggested to select patients for more frequent surveillance and further testing (such as cross-sectional imaging). In the unexposed population (without metal-on-metal prostheses), the upper limit of the reference range for both cobalt and chromium ion levels is  $0.5 \mu\text{g/L}$ <sup>7</sup>. The authors of small studies have reported average whole blood levels of 1 to 2  $\mu\text{g/L}$  for patients with well-functioning metal-on-metal hip implants<sup>8</sup> and higher levels in patients with failed metal-on-metal hip arthroplasties<sup>9</sup>. The MHRA action level provided a specificity of 89% and a sensitivity of 52% for detecting a preoperative, unexplained failed metal-on-metal hip resurfacing<sup>10</sup>, but to our knowledge no authors have reported diagnostic test characteristics of blood metal ion levels following metal-on-metal total hip arthroplasties. Further, the results in recent studies comparing metal ion levels following hip resurfacing with those following large-diameter total hip arthroplasty are conflicting (see [Appendix](#))<sup>11-14</sup>.

We recognize from our own practice and the existing literature that the decision to revise a metal-on-metal hip is not always straightforward. For instance, hip pain may be due to problems in other anatomical locations and consequently hip function scores do not quantify hip function alone. Tests for blood metal ion levels are now routinely available in many countries and at modest cost. The aim of this study was to determine the value of whole blood metal ion levels in predicting failure for both hip resurfacing and large-diameter total hip implants.

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## **LL MATERIALS AND METHODS**

### **Study Design**

We performed a prospective study involving 597 consecutive patients with current-generation, unilateral

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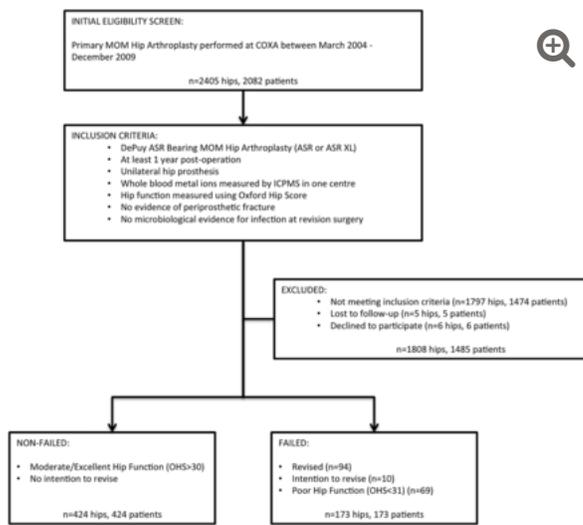
metal-on-metal hip replacements from one center. Institutional review board approval was obtained (number R11006, Pirkanmaa Hospital District ethics committee).

### **Inclusion Criteria**

From March 2004 to December 2009, 2082 patients (2405 hips) underwent metal-on-metal hip replacements at our institution. During the same time period, Articular Surface Replacement (ASR; DePuy Orthopaedics, Warsaw, Indiana) metal-on-metal hip replacements were used in 1036 (43%) operations (887 patients). The choice regarding the type of metal-on-metal hip replacement used was based on the surgeon's preference. DePuy Orthopaedics voluntarily recalled its ASR metal-on-metal hip system in August 2010, and the MHRA announced a medical device alert regarding ASR hip arthroplasty implants in September 2010. After the announcement, our institution established a surveillance program to identify possible articulation-related complications in patients who had received either an ASR hip resurfacing implant or an ASR XL total hip replacement at our institution. All patients received an Oxford Hip Score questionnaire, underwent clinical examination, and underwent measurement of whole blood cobalt and chromium ion levels.

Anteroposterior and lateral radiographs of the hip and an anteroposterior pelvic radiograph were made at each visit. All patients had metal artifact reduction sequence magnetic resonance imaging (MRI). Five patients (0.6%) were lost to follow-up when they went abroad. Patients were recruited from October 2010 to December 2011. Six patients (0.7%) declined to participate.

We included all patients who had given informed consent and who had unilateral, current-generation, large-diameter (head size >36 mm) metal-on-metal hip arthroplasty; whole blood metal ion levels that were measured more than twelve months following the primary surgery; and hip function recorded with use of the Oxford Hip Score ([Fig. 1](#)). Thirty-nine cases scored only with the Harris hip score were excluded.



**Fig. 1** [Open in new tab](#) | [Download powerpoint](#)

Study flowchart. MOM = metal-on-metal, COXA = Coxa Hospital for Joint Replacement, ASR = Articular Surface Replacement, ICPMS = inductively coupled plasma mass spectrometry, and OHS = Oxford Hip Score.

## Exclusion Criteria

Patients who underwent revision arthroplasty for a microbiologically confirmed infection and/or a periprosthetic fracture were excluded.

## Definitions

We defined implant failures ( $n = 173$ ) as prostheses that subsequently underwent revision, those for which a revision was planned, and those associated with a poor Oxford Hip Score<sup>45</sup> ( $<31$  of 48). We defined non-failed implants ( $n = 424$ ) as those in patients with at least moderate hip function (Oxford Hip Score,  $\geq 31$  of 48). Findings on clinical history, physical examination, radiographs, and metal artifact reduction sequence MRI were used in the decision whether to revise, while blood metal ion results were not used to make this revision decision. Four patients awaiting revision had excellent patient-reported hip function scores (Oxford Hip Score,  $>41$ ), but all patients had accepted criteria for revision: mechanical symptoms (creaking), a solid pseudotumor, “pressure symptoms” in the hip, and a cystic pseudotumor. We included the maximum value of blood metal ions as a separate variable in the analysis because the MHRA guidelines do not distinguish between cobalt and chromium. Therefore, Max (Co, Cr) is the maximum value of either whole blood cobalt or chromium ions.

## **Analysis of Cobalt and Chromium Ion Levels**

Blood was sampled from the antecubital vein with use of a BD Vacutainer blood collection set (Beckton, Dickson) and blood collection tubes containing sodium EDTA (ethylenediaminetetraacetic acid) or heparin for trace element testing. Researchers at the Finnish Institute for Occupational Health used dynamic reaction cell inductively coupled plasma (quadripole) mass spectrometry (Agilent 7500cx; Agilent Technologies, Santa Clara, California) of whole blood. This method was validated with previously published methods<sup>16</sup> following a blinded, interlaboratory study. Whole blood metal ion measurement was performed at the same time as clinical scoring.

### **Power Analysis**

We based our power calculations on the aim of detecting a significant difference in sensitivity between the cutoff at about 5 and 7 µg/L. We used previous findings on sensitivity (52% for 7.2 µg/L and 63% for 4.8 µg/L)<sup>10</sup> and the McNemar test to identify whether there is a significant difference in sensitivities between those values. We used a significance level of 0.05 and a number of implant failures of 173, and we chose an average probability of disagreement between the diagnostic tests (0.3). Power calculation indicated 84% power to detect a significant difference in sensitivity between the two diagnostic tests.

### **Statistical Methods**

Stata statistical software (release 12; StataCorp) was used for statistical analyses. Chromium and cobalt measures were not normally distributed; therefore, nonparametric tests were used for comparisons. A p value of <0.05 was considered significant. Receiver operating characteristic curves for cobalt, chromium, and the maximum between them were constructed to test discriminant ability between failed and non-failed implants. Sensitivity, specificity, positive and negative predictive values, and misclassification rate were calculated for different cutoff levels of blood metal ions. Areas under the receiver operating characteristic curves were compared with use of chi-square tests to identify differences in discriminant power between metal ion thresholds. A multiple logistic regression model was fitted to measure the effects of cobalt, chromium, or the

maximum between them and patient characteristics (age, sex, implant type, and time since the primary surgery) on hip function. Chromium and cobalt were not fitted in the model together to avoid multicollinearity (correlation [Cr, Co] = 0.9). Nonlinearity and non-additivity were explored and a model was chosen to maximize the explanatory power, taking into account the predictive ability of the model. When an interaction with a categorical factor was detected, the receiver operating characteristic curve analyses were repeated separately by categories of that factor. Micrograms per liter is interchangeable with parts per billion and can be converted to nmol/L with use of the following equations: (a) (cobalt value in  $\mu\text{g/L}$ )  $\times$  1000/59, and (b) (chromium value in  $\mu\text{g/L}$ )  $\times$  1000/53.

### Source of Funding

There was no external funding source.

## RESULTS

Five hundred and ninety-seven patients met our entry criteria ([Fig. 1](#) and [Table I](#)).

TABLE I

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Demographics of the Patients Included in the Study\*

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### Metal Ion Levels

The median whole blood metal ion level in patients with non-failed hip implants was 1.6  $\mu\text{g/L}$  for cobalt and 1.6  $\mu\text{g/L}$  for chromium (1.9  $\mu\text{g/L}$  for Max [Co, Cr]). Failed hips had median values of 7  $\mu\text{g/L}$  for cobalt and 2.6  $\mu\text{g/L}$  for chromium (7  $\mu\text{g/L}$  for Max [Co, Cr]). In failed arthroplasties, median cobalt, chromium, and Max (Co, Cr) values were all significantly higher than for non-failed arthroplasties (all  $p < 0.01$ ) ([Table II](#)).

TABLE II

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Descriptive Statistics for Whole Blood Metal Ion Levels\*

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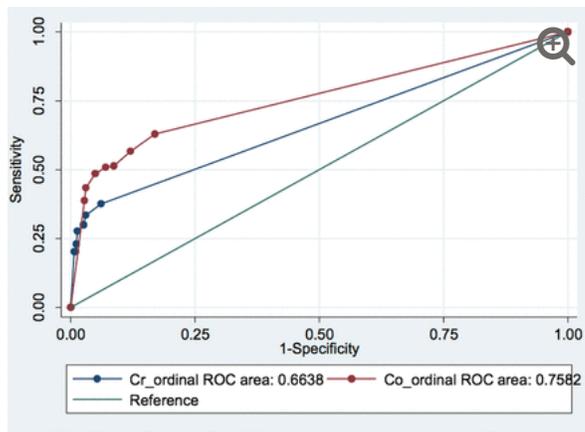
In failed arthroplasties, median blood chromium values were not significantly different for hip resurfacing and total hip arthroplasty ( $p = 0.058$ ). However, blood cobalt values and Max (Co, Cr) were significantly higher for

total hip arthroplasties ( $p = 0.018$  and  $0.030$ , respectively).

In non-failed arthroplasties, a similar pattern was observed for hip resurfacing and total hip arthroplasty; there was no difference for chromium ( $p = 0.41$ ), and cobalt and Max (Co, Cr) values were significantly higher for total hip arthroplasties ( $p < 0.0001$  for both).

### **Diagnostic Test Characteristics and Receiver Operating Characteristic Curves**

Diagnostic test characteristics were similar for cobalt and Max (Co, Cr), while chromium tended to yield less effective discrimination, as shown in a plot allowing comparison of cobalt with chromium for selected cutoffs above and below the recommended cutoff of  $7 \mu\text{g/L}$  (**Fig. 2**), with the area under the curve for individual cutoffs ranging from 0.63 to 0.76. Overall, for the selected cutoffs, use of the Max (Co, Cr) yielded a very similar area under the curve as cobalt alone and the same as the  $7 \mu\text{g/L}$  cutoff. A higher cutoff increased the specificity but decreased the sensitivity. A cutoff of  $10 \mu\text{g/L}$  provided nearly perfect overall specificity (97%; 95% confidence interval [CI], 95% to 98%) but low sensitivity (39%; 95% CI, 32% to 46%) for Max (Co, Cr). Seven micrograms per liter provided good overall specificity (93%; 95% CI, 90% to 95%) but poor sensitivity (51%; 95% CI, 43% to 59%), with an area under the curve of 0.72. The area under the curve for thresholds at 4 and  $5 \mu\text{g/L}$  of Max (Co, Cr) were virtually the same (0.724) and were slightly larger than but not significantly different from ( $p$  values = 0.72 and 0.67, respectively) the threshold at  $7 \mu\text{g/L}$ . The  $7\text{-}\mu\text{g/L}$  cutoff had a positive predictive value of 0.75 (95% CI, 0.66 to 0.82) and a negative predictive value of 0.82 (95% CI, 0.78 to 0.86). **Table III** and a table in the electronic **Appendix** show the effects of different metal ion cutoff levels and predictive values for the  $7\text{-}\mu\text{g/L}$  cutoff.



**Fig. 2** [Open in new tab](#) | [Download powerpoint](#)

Receiver operating characteristic (ROC) curve showing the abilities of cobalt (Co) and chromium (Cr) levels to discriminate failed from non-failed metal-on-metal hip implants.

**TABLE III** [View popup](#) | [View inline](#)

Positive and Negative Predictive Values for the Cutoff of Seven Micrograms per Liter of Cobalt\*

### Logistic Regression Analysis

The significant predictors for hip failure were Max (Co, Cr) and the interaction between metal ion and implant type ( $p < 0.001$ ). For patients managed with total hip arthroplasty, for a unit increase in metal ions, there was a 23% increase in the odds of being in the failed group. However, there was only a 5% increase in the odds for patients managed with hip resurfacing. This interaction between Max (Co, Cr) levels and implant type was virtually the same as the interaction between cobalt alone and implant type (odds ratio [OR] = 1.23 for total hip arthroplasty and 1.05 for hip resurfacing;  $p < 0.001$ ). For chromium alone, the interaction with implant type was significant but implant type was also significant (OR = 0.44); that is, the odds of a failed hip in patients managed with total hip arthroplasty are 2.3 times higher than those in patients managed with hip resurfacing ( $p = 0.009$ ). Age was not significant and did not appear to confound the association between the ion level and hip failure. Female sex showed a moderate increase in the odds of poor hip function, as did an additional year since primary surgery; as they did not appear to confound the association with hip failure, they were removed from the model. The results of the logistic regression analysis are presented in [Table IV](#).

### Stratified Analysis by Implant Type

Hip resurfacings and total hip arthroplasties had different effects on blood metal ion levels. The prevalence of hip failure was 0.16 in patients managed with hip resurfacing and 0.40 in those managed with total hip arthroplasty. The specificity and sensitivity of both cobalt and Max (Co, Cr) at 7 µg/L for predicting hip failure were 87% (95% CI, 81% to 91%) and 55% (95% CI, 46% to 64%) in total hip arthroplasty, and they were 98% (95% CI, 95% to 99%) and 39% (95% CI, 25% to 55%) in hip resurfacing. The specificity and sensitivity for chromium at 7 µg/L were 99% (95% CI, 96% to 100%) and 26% (95% CI, 19% to 35%) for total hip arthroplasty, and they were 98% (95% CI, 95% to 99%) and 33% (95% CI, 20% to 48%) for hip resurfacing. Thus, for hip resurfacing it appears that the performance of the diagnostic test with Max (Co, Cr) (which at 7 µg/L is the same as that for cobalt alone) is very similar to performance of the diagnostic test with chromium alone. However, for total hip arthroplasty, the performance of the diagnostic test differs even more markedly for chromium and cobalt than in the analysis combining total hip arthroplasty and hip resurfacing implants. This reflects a different distribution and role in the prediction of hip failure for cobalt and chromium in total hip arthroplasty and hip resurfacing, with cobalt and chromium having a more similar distribution in hip resurfacing than in total hip arthroplasty. Although the misclassification rates are nearly optimal at 7 µg/L for Max (Co, Cr) for both total hip arthroplasty and hip resurfacing (26% and 12%), a lower threshold for hip resurfacing would allow a better balance between sensitivity and specificity.

### LL DISCUSSION

The results of this study have confirmed that blood metal ions are significantly higher in patients with failed compared with non-failed metal-on-metal hip arthroplasties. We believe that this is the first study to identify this separately for both hip resurfacing and total hip arthroplasty. Blood metal ion measurement is now so commonly performed that the recruitment of large

numbers of patients for studies to support the findings in existing, smaller studies is justified. Approximately 93,000 patients worldwide received a DePuy Articular Surface Replacement hip prosthesis<sup>17</sup>. Elevated blood metal ion levels have excellent specificities and good positive predictive values for detecting failed metal-on-metal hip arthroplasties and may be used to select patients for the closest surveillance. However, blood metal ion levels have poor sensitivities and should not be used in isolation to select patients for clinical follow-up. No level had a perfect positive predictive value, and so we cannot recommend revision surgery based on raised blood metal ion levels in the absence of clinical symptoms or evidence of soft-tissue disease on cross-sectional images. However, we recognize reports of the adverse effects of high levels of circulating metal ions from hip replacements on the nervous system<sup>18</sup> and their association with auditory and visual impairment<sup>19</sup>, poor concentration<sup>20</sup>, and cardiomyopathy<sup>21</sup>. We recommend a low threshold for investigation of systemic symptoms.

For the MHRA action level of 7 µg/L<sup>6</sup>, we found an overall sensitivity of 51% and a specificity of 93% for separating failed from moderately and well-functioning metal-on-metal hip arthroplasties. We suggest that there is no safe lower level for blood metal ions, so all symptomatic patients should undergo a clinical history, physical examination, testing for baseline blood metal ion levels, and serial radiography to identify non-hip pathologies, infection, fracture, and component misalignment and loosening. We have a low threshold for ordering cross-sectional imaging of patients with symptoms who present to our centers<sup>22</sup>. In our practice, patients with metal-on-metal hip arthroplasties are referred for cross-sectional imaging if they have hip symptoms or even slightly elevated blood metal ion levels (>7 µg/L). We use metal artifact reduction sequence MRI to identify inflammatory lesions and musculotendinous pathologies, while other authors have successfully used ultrasound<sup>23</sup>.

The presence of an interaction between implant type and metal ions led us to investigate the use of metal ion levels as a diagnostic test, separately, in total hip arthroplasty and hip resurfacing implant types. In hip resurfacing, the performances of chromium and cobalt levels as diagnostic tests were much more similar than

they were in total hip arthroplasty. Cobalt ion levels were raised out of proportion to chromium ion levels in failed total hip arthroplasty, which may reflect a different mechanism for metal ion generation. However, the reduced cohort size in the implant type-stratified analyses might hinder the generalizability of the performance of the ion-level diagnostic tests beyond this cohort. More generally, the smaller size of the subgroup analyses suggests that, for the purpose of predicting hip failure, a model-based procedure derived on the entire data set should be used. This would simultaneously take into account the multivariate data available on the patients to maximize the area under the curve, instead of using the metal ion dimension only (which nonetheless retains its appeal for its simplicity to aid in decision-making).

### **Strengths and Limitations of the Study**

To our knowledge, this is the first prospective, single-center cohort study to investigate the ability of blood metal ion levels to discriminate metal-on-metal hip arthroplasties according to clinical status for both total hip arthroplasty and hip resurfacing devices. A limitation is that we have made only a single-point assessment of patients. However, we have attempted to reduce this uncertainty by choosing to categorize our groups using a cutoff value of a hip score of 31 (of 48). (Note that the median Oxford Hip Score for patients undergoing hip replacement in the United Kingdom is 18 of 48.) This cutoff value of 31 divides our patients into two groups: those with failed hips and those with moderately or well-functioning hips. We plan to follow patients with moderate function.

Testing for blood metal ion measurement is widely available, inexpensive, and non-invasive<sup>24</sup>. In the United Kingdom, the MHRA supports a Supra Regional Assay Service so that cobalt and chromium measurement is included in the monthly Trace Element Quality Assessment Scheme, which requires interlaboratory analysis and a standard that all laboratories use for analysis and reporting of values. In the current study, we used a validated measurement method for blood metal ion analyses. To make the results of different studies comparable, it is crucial that all laboratories analyzing blood metal ion samples also use validated methods. Future research is warranted to determine

whether blood metal ion levels have similar diagnostic test characteristics in patients with metal-on-metal hip arthroplasty designs other than those analyzed in the current study.

We recommend that future work focus on determining whether blood metal ion levels are able to predict soft-tissue damage, because such a prediction would trigger a decision to revise. To achieve this prediction, there needs to be a consensus on the interpretation of metal artifact reduction sequence MRI, such as on the clinical meaning of a cystic pseudotumor, which may be found in patients with well-functioning metal-on-metal implants.

Revision surgery, or intention to revise (if surgery is pending), is the most important determinant in the fate of these devices. Patient-reported hip-function scores, which are variable and have inherent limitations, were not used as the sole assignment tool in our allocation of patients. Importantly, our decision to revise was not based on blood metal ion measurements.

### **Comparison with Other Studies**

There is no report that we are aware of on the specificity and sensitivity of whole blood metal ion levels in detecting failed metal-on-metal total hip arthroplasties. Blood metal ion measurement has previously been shown to have good discriminant ability for failed and well-functioning hip resurfacings<sup>10</sup> and modest discriminant ability in symptomatic patients for diagnosis of adverse responses to metal debris on MRI<sup>25</sup>. Our study has demonstrated that blood metal ion levels are a useful tool for detecting failed metal-on-metal total hip arthroplasties. To our knowledge, this is also the first and only study to demonstrate a difference in diagnostic test characteristics of blood metal ion levels between hip resurfacings and total hip arthroplasties.

#### *Suggested Specific Uses of Blood Metal Ion Measurement*

*Diagnosis:* Is the pain coming from the periprosthetic area? Hip function scores may be degraded by many other parameters, including referred pain and psychological factors. Blood metal ion measurement represents a useful confirmatory test that aids the

clinician in deciding which patients to refer for cross-sectional imaging.

*Prognosis:* We have demonstrated and quantified the association of metal ion levels with poor function and the need for revision surgery. A prospective study with a cohort of this magnitude that quantifies risk for revision surgery for a given metal ion measurement does not yet exist. The data presented in this study serve as a useful approximation in the interim. A number of reports have presented metal ion levels in patients managed with metal-on-metal hip arthroplasties (see [Appendix](#)). It is difficult to directly compare these studies because of the heterogeneity in assays, analysis (whole blood or serum), study design and patient demographics, and types of hip implants. In patients with well-functioning metal-on-metal hip resurfacing prostheses, median reported cobalt ion values ranged from 0.54 µg/L<sup>11</sup> to 4.28 µg/L<sup>7</sup> and chromium ion values ranged from 0.84 µg/L<sup>11</sup> to 5.12 µg/L<sup>7</sup>. In patients with well-functioning large-diameter total hip prostheses, median reported cobalt ion values ranged from 0.94 µg/L<sup>8</sup> to 5.38 µg/L<sup>11</sup> and chromium ion values ranged from 1.22 µg/L<sup>7</sup> to 2.88 µg/L<sup>11</sup>. One study showed good discriminant ability for well-functioning and failed metal-on-metal hip arthroplasties<sup>10</sup>. In the current study, the results agree with this finding and show similar diagnostic test characteristics for different blood metal ion cutoff levels.

## **LL CONCLUSIONS AND POLICY IMPLICATIONS**

Raised blood metal ion levels were associated with failed metal-on-metal hip resurfacing and total hip arthroplasties. A threshold level of 7 µg/L had inadequate sensitivity to be used in isolation as a screening test for implant failure, but it provided nearly optimal misclassification rates. No level had a perfect positive predictive value. Therefore, we discourage surgeons from performing revision surgery based on blood metal ion levels alone. Cobalt ion levels were raised out of proportion to chromium ion levels in failed total hip arthroplasty, which may reflect a different mechanism for metal ion generation.

## **LL APPENDIX**

A table showing a summary of studies comparing blood metal ion levels in patients with hip resurfacing and large-diameter metal-on-metal total hip implants as well

as a table showing diagnostic test characteristics for categorizing hips as either poor-functioning or well-functioning with use of different cutoff levels of blood metal ions are available with the online version of this article as a data supplement at [jbj.s.org](http://jbj.s.org).

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## **LL FOOTNOTES**

- Investigation performed at Coxa Hospital for Joint Replacement, Tampere, Finland
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